

REMARKS

I. Status of the Claims

Claims 1-23 were originally filed and later canceled. Claims 24-28 have been added and are currently pending under examination. Claim 26 is amended to recite " α -actin" in place of ".alpha.-actin" to correct a typographic impropriety. No new matter is introduced.

II. Specification

The specification is amended to recite priority information, as well as to correct description of Figures 2 and 3, which was mismatched with the contents of Figures 2 and 3. No new matter is introduced by the present amendment.

III. Claim Rejections

A. Double Patenting

Claims 24-28 were rejected under the judicially created doctrine of obviousness-type of double patenting as allegedly being unpatentable over claims 1, 3, 4, 8, and 10 of U.S. Patent No. 6,371,992. Specifically, the Examiner stated that the pending claims, directed to matrix graft derived from ureter or urethra smooth muscle tissue, are not patentably distinct from the issued claims, directed to matrix graft is derived from bladder smooth muscle tissue, because the two types of smooth muscle are similar. Applicants are willing to consider filing a terminal disclaimer once the claims are found otherwise allowable.

B. 35 U.S.C. §102

Claims 24-28 were also rejected under 35 U.S.C. §102(e) for alleged anticipation by Gregory (U.S. Patent No. 5,990,379). Applicants respectfully traverse the rejection.

To anticipate a pending claim, a prior art reference must provide, either expressly or implicitly, each and every limitation of the pending claim. MPEP §2131. The pending claims are drawn to an insoluble elastic matrix graft for repairing ureter or urethra smooth muscle. This matrix graft is derived from ureter or urethra smooth muscle tissue, impermeable to urine, consists essentially of an intact framework of collagen and elastic fibers, which is free of cell

contents and permits growth of muscle cells within. In other words, the claimed matrix graft retains the collagen/elastin scaffolding that naturally exists in ureter or urethra smooth muscle tissue.

In contrast, the Gregory reference relates to a prosthetic device comprising a support member (which comprises a stent, a conduit, or a scaffold) and a layer of elastin-based material located on the support member. The matrix described by Gregory is an elastin matrix, not a collagen/elastin matrix. There is no indication that Gregory's method preserves the natural collagen/elastin matrix. In fact, as discussed below in more detail, the conditions used by Gregory to extract elastin are too harsh to avoid the degradation of collagen and the consequent destruction of the natural scaffolding of collagen and elastin.

In the claimed network of interwoven collagen and elastin fibers, collagen imparts strength and elastin imparts flexibility. As established by evidence of record, collagen is a fibrous protein that is readily solubilized under conditions where elastin is not solubilized appreciably. The Furuto reference (A2 of the IDS filed January 18, 2002) describes, on pages 43-44, a preferred method for solubilizing collagens. Selective extraction of collagen involves using salt and diluted acid. Elastin and its purification procedures are described in the Rosenbloom reference (A3 of the IDS) and the Soskel reference (A4 of the IDS). According to the Rosenbloom article, the fibers of elastin (or elastic fibers) are 90% elastin and 10% microfibrillar component. Soskel *et al.* describe on page 196 that elastin is a polymer of "heavily cross-linked mesh work" and more "a fiber rather than a protein." The elastin extraction method described by Gregory in column 5, lines 36-55, employs treatment involving acid, base, heat, *etc.* These harsh conditions are effective for elastin purification but do not allow the preservation of collagen or microfibrillar components, and hence do not allow the preservation of the natural scaffolding of collagen/elastin, which is one of the important features of the subject matter of the pending claims in this application.

Because the Gregory reference does not teach preparing a collagen/elastin matrix that retains the naturally occurring fiber framework found in ureter or urethra smooth muscle

tissue, this reference cannot anticipate the pending claims. Withdrawal of the §102 rejection based on Gregory is therefore respectfully requested.

C. 35 U.S.C. §103

Probst et al.

Claims 24-28 were rejected under 35 U.S.C. §103(a) for alleged obviousness over Probst *et al.* Applicants respectfully traverse the rejection.

In order to qualify as the basis of a §103(a) rejection, a reference must meet the requirement of §102 with the exception of not having all claim limitations. As far as the Probst reference is concerned, it meets the requirement of none of §102(a)-(g), since it is a non-patent publication describing the work by the inventors on the present application and was not published more than one year prior to the effective filing date of this application, December 19, 1997. Specifically, a copy of a Katz declaration by inventors Drs. Tanagho, Dahiya, Lue, and Cunha is attached. This declaration was initially filed on October 5, 2001, during prosecution of the parent application USSN 08/994,838, and establishes that the Probst reference is not one reflecting an invention by "others."

Therefore, the Probst *et al.* reference is not available as a prior art reference and cannot support a rejection for obviousness. The §103 rejection based on Probst *et al.* is therefore improper and its withdrawal is respectfully requested.

Gregory in Light of Bishopric et al. or Goldstein et al. or Abraham et al.

Claims 24-28 were further rejected under 35 U.S.C. §103(a) for alleged obviousness over Gregory in light of Bishopric *et al.* (U.S. Patent No. 5,855,620) or Goldstein (U.S. Patent No. 5,632,778) or Abraham *et al.* (U.S. Patent No. 5,993,844). Applicants respectfully traverse the rejection.

First of all, Applicants contend that Abraham *et al.* is not available as a prior art reference, since the present inventors had completed the subject invention prior to the effective filing date of the Abraham patent, May 8, 1997. Attached is a copy of a declaration pursuant to 37 C.F.R. §1.131 by inventors Drs. Tanagho and Dahiya, which was initially filed on May 9,

2001, for the parent application USSN 08/994,838, along with Exhibit 1, which is a copy of the cover of *British Journal of Urology*, which contains the Probst reference, bearing a library stamp dated May 2, 1997. This declaration and its exhibit establish that the underlying invention of the present application was accomplished in the United States and prior to May 8, 1997. Applicants thus respectfully request that the obviousness rejection based on Gregory in light of Abraham *et al.* be withdrawn.

In order to establish a *prima facie* showing of obviousness, three requirements must be satisfied: all limitations of a pending claim must be expressly or impliedly disclosed by prior art references; there must be a suggestion or motivation in the art for one skilled artisan to combine the limitations; and there must be a reasonable expectation of success in making such a combination. MPEP §2143. As discussed above, the Gregory reference does not supply all claim limitations, for instance, the limitation that an intact collagen/elastin network naturally present in the ureter or urethra smooth muscle tissue is preserved. This limitation is apparently supplied by the Bishopric *et al.* reference, which describes a general collagen/elastin matrix produced from tissues such as heart valves. Similarly, the Goldstein reference describes bioprosthesis derived from tissues following a decellularizing process. The tissue types discussed in this reference are skin and heart valves. On the other hand, Gregory names ureter as a possible tissue source for preparing elastin matrix.

A review of the three references, however, fails to reveal any suggestion or motivation for one of skill in the art to combine the limitations. As stated above, Gregory teaches extraction of elastin in a process far too harsh to preserve the intact collagen/elastin scaffolding. An artisan who sets out to prepare a bioprosthesis described by Bishopric or Goldstein would unlikely combine the disclosure of Gregory, as it teaches the disruption of the fibrous network and therefore defeats the purpose of preparing a implantable material having required structural integrity.

Even if an artisan were somehow inspired to combine the teachings of Gregory and Bishopric or Goldstein, and attempted to produce a collagen/elastin matrix derived from tissues other than those actually experimented by Bishopric and Goldstein, namely heart valves

and skin, there would be no reasonable expectation of success in achieving such a matrix with the properties as defined in claim 24. This is because the large number of different types of tissues present in a human body, which differ drastically in terms of strength, elasticity, and porosity of the cellular matrix. Heart valves are a type of highly specialized tissue in that the tissue is nearly acellular except for a thin external layer of cells that can be readily removed by a variety of treatment methods to achieve a thick, dense, and relatively stiff matrix. In contrast, the intact matrix of smooth muscle such as that forms ureter or urethra provides a waterproof sheath with much higher flexibility. The matrix taught by Bishopric or Goldstein cannot substitute the matrix provided by the present disclosure. Nor can a matrix produced from any randomly selected tissue type be expected to achieve the exceptional properties of the matrix of the present invention, which are essential for repairing ureter or urethra.

Because the references provide no suggestion or motivation to combine the claim limitations that might be found in the references, and there is certainly no reasonable expectation that such combination would produce a collagen/elastin matrix having the property of water impermeability and susceptibility for muscle cell repopulation, Applicants submit that no *prima facie* case of obviousness is established. Accordingly, the withdrawal of the §103 rejection based on Gregory in light of Bishopric *et al.* or Goldstein is respectfully requested.

Appl. No. 10/052,889
Amdt. dated July 14, 2004
Reply to Office Action of February 25, 2004

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Chuan Gao
Reg. No. 54,111

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments (copy of Katz declaration; copy of §1.131 declaration with Exhibit 1)
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